

# SEQUENCE LISTING

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<120> BLOOD-BRAIN BARRIER THERAPEUTICS

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<170> PatentIn version 3.0

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<211> 6

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (6)..(6)

<223> Polymer connected to epsilon-amino group

<400> 1

Tyr Gly Gly Phe Met Lys

1

5

<210> 2

<211> 6

<212> PRT

<213> synthetic construct

<220>

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<222> (1)..(1)  
<223> Polymer connected to alpha-amino group

<220>  
<221> MOD\_RES  
<222> (6)..(6)  
<223> Polymer connected to epsilon-amino group

<400> 2

Tyr Gly Gly Phe Met Lys  
1 5

<210> 3  
<211> 6  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Polymer connected to alpha-amino group

<400> 3

Tyr Gly Gly Phe Met Lys  
1 5

<210> 4  
<211> 6  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> ACETYLATION

<220>  
<221> MOD\_RES  
<222> (6)..(6)

<223> AMIDATION

<400> 4

Phe Arg Trp Trp Tyr Lys  
1 5

<210> 5

<211> 6

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (1)..(1)

<223> ACETYLATION

<220>

<221> MOD\_RES

<222> (6)..(6)

<223> AMIDATION

<400> 5

Arg Trp Ile Gly Trp Lys  
1 5

<210> 6

<211> 6

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (6)..(6)

<223> AMIDATION

<220>

<221> UNSURE

<222> (6)..(6)

<223> Xaa can be any of the twenty naturally occurring

amino acids

<400> 6

Trp Trp Pro Lys His Xaa  
1 5

<210> 7

<211> 4

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (4)..(4)

<223> AMIDATION

<220>

<221> UNSURE

<222> (4)..(4)

<223> Xaa is either Lys or Arg

<400> 7

Trp Trp Pro Xaa  
1

<210> 8

<211> 6

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (6)..(6)

<223> AMIDATION

<220>

<221> UNSURE

<222> (6)..(6)

<223> Xaa can be any one of the naturally occurring ami

no acids

<400> 8

Tyr Pro Phe Gly Phe Xaa  
1 5

<210> 9

<211> 7

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (1)..(5)

<223> Amino acids are in the D-form

<220>

<221> MOD\_RES

<222> (6)..(6)

<223> n is 0 or 1

<220>

<221> MOD\_RES

<222> (7)..(7)

<223> Xaa is Gly or the D-form of a naturally occurring amino acid

<220>

<221> MOD\_RES

<222> (7)..(7)

<223> AMIDATION

<400> 9

Ile Met Ser Trp Trp Gly Xaa  
1 5

<210> 10

<211> 6

<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(4)  
<223> Amino acids are in the D-form

<220>  
<221> MOD\_RES  
<222> (6)..(6)  
<223> Xaa is Gly or the D-form of a naturally-occurring amino acid

<220>  
<221> MOD\_RES  
<222> (6)..(6)  
<223> AMIDATION

<400> 10

Ile Met Thr Trp Gly Xaa  
1 5

<210> 11  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is A1, wherein A1 is the D-form of Nve or Nle

<220>  
<221> MOD\_RES  
<222> (3)..(3)  
<223> Xaa is B2, wherein B2 is Gly, Phe, or Trp

<220>

<221> MOD\_RES  
<222> (4)..(4)  
<223> Xaa is C3, wherein C3 is Trp or Nap

<220>  
<221> MOD\_RES  
<222> (4)..(4)  
<223> AMIDATION

<400> 11

Tyr Xaa Xaa Xaa  
1

<210> 12  
<211> 3  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr has at its N-terminus an Me-x-H-y-N group, wherein x is 0, 1, or 2; and y is 0, 1, or 2, with the proviso that x and y is never greater than

<220>  
<221> MOD\_RES  
<222> (1)..(2)  
<223> The amine between the first Tyr and the second Tyr is methylated

<220>  
<221> MOD\_RES  
<222> (3)..(3)  
<223> Xaa is Xaa-z, wherein Xaa is Phe, (D)Phe, or NHBz, and wherein z is 0 or

<220>  
<221> MOD\_RES  
<222> (3)..(3)  
<223> AMIDATION

<400> 12

Tyr Tyr Xaa  
1

<210> 13  
<211> 6  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (4)..(4)  
<223> Xaa is D4, wherein D4 is Lys or Arg

<220>  
<221> MOD\_RES  
<222> (5)..(5)  
<223> His is His-z, wherein z is 0 or 1

<220>  
<221> MOD\_RES  
<222> (6)..(6)  
<223> Xaa is Xaa-z, wherein Xaa is a naturally occurring amino acid and  
z is 0 or

<220>  
<221> MOD\_RES  
<222> (6)..(6)  
<223> AMIDATION

<400> 13



Trp Trp Pro Xaa His Xaa  
1 5

<210> 14  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 14

Tyr Xaa Phe Phe  
1

<210> 15  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (4)..(4)  
<223> AMIDATION

<400> 15

Tyr Xaa Phe Phe  
1

<210> 16

<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is Tyr(N-alpha-Me), i.e. N-alpha-methyltyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 16

Tyr Xaa Phe Phe  
1

<210> 17  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is Tyr(N-alpha-Cmp), i.e. N-alpha-cyclopropyl methyltyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 17

Tyr Xaa Phe Phe

1

<210> 18  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is Tyr(N-alpha-Hex), i.e. N-alpha-hexyltyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 18

Tyr Xaa Phe Phe  
1

<210> 19  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is Tyr(N-alpha-Et2), i.e. N-alpha-diethyltyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 19

Tyr Xaa Phe Phe  
1

<210> 20  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 20

Tyr Xaa Phe Phe  
1

<210> 21  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (4)..(4)  
<223> AMIDATION

<400> 21

Tyr Xaa Phe Phe  
1

<210> 22  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is H-Tyr(3-F), i.e. 3-fluorotyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 22

Tyr Xaa Phe Phe  
1

<210> 23  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is H-Tyr(3-Cl), i.e. 3-Chlorotyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 23

Tyr Xaa Phe Phe  
1

<210> 24  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is H-Tyr(3-Br), i.e. 3-bromotyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 24

Tyr Xaa Phe Phe  
1

<210> 25  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinolin

<220>  
<221> MOD\_RES  
<222> (2)..(3)  
<223> nonpeptidyl bond

<400> 25

Tyr Xaa Phe Phe  
1

<210> 26  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(3)  
<223> nonpeptidyl bond

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinolin

<220>  
<221> MOD\_RES  
<222> (4)..(4)  
<223> AMIDATION

<400> 26

Tyr Xaa Phe Phe  
1

<210> 27  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinoline

<220>  
<221> MOD\_RES  
<222> (3)..(3)  
<223> Phe is -NCH3]Phe, i.e. N-methylphenylalanine

<400> 27

Tyr Xaa Phe Phe  
1

<210> 28  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinoline



ahydroisoquinoli  
n

<220>  
<221> MOD\_RES  
<222> (3)..(3)  
<223> Phe is -NH]Hfe, i.e. homophenylalanine

<400> 28

Tyr Xaa Phe Phe  
1

<210> 29  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr is Tyr(NMe), i.e. N-methyltyrosine

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetr  
ahydroisoquinoli  
n

<220>  
<221> MOD\_RES  
<222> (3)..(3)  
<223> Phe is -NH]Hfe, i.e. homophenylalanine

<400> 29

Tyr Xaa Phe Phe  
1

<210> 30  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3  
-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (3)..(3)  
<223> Gly is Phg, i.e. phenylglycine

<400> 30

Tyr Xaa Gly Phe  
1

<210> 31  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3  
-carboxylic acid

<400> 31

Tyr Xaa Trp Phe  
1

<210> 32  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3  
-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (4)..(4)  
<223> AMIDATION

<400> 32

Tyr Xaa Trp Phe  
1

<210> 33  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3  
-carboxylic acid

<400> 33

Tyr Xaa His Phe  
1

<210> 34  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3  
-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (3)..(3)  
<223> Ala is 2-Nal, i.e. 3-(2'-naphthyl)alanine

<400> 34

Tyr Xaa Ala Phe  
1

<210> 35  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (3)..(3)  
<223> Xaa is Atc, i.e. 2-aminotetralin-2-carboxylic acid

<400> 35

Tyr Xaa Xaa Phe  
1

<210> 36  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (4)..(4)

<223> Phe is Phe(pNO2), i.e. 4-nitrophenylalanine

<400> 36

Tyr Xaa Phe Phe

1

<210> 37

<211> 4

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (4)..(4)

<223> Phe is Phe(pNO2), i.e. 4-nitrophenylalanine

<400> 37

Tyr Xaa Trp Phe

1

<210> 38

<211> 4

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (4)..(4)  
<223> AMIDATION

<400> 38

Tyr Xaa Phe Trp  
1

<210> 39  
<211> 7  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (7)..(7)  
<223> AMIDATION

<400> 39

Tyr Xaa Phe Phe Val Val Gly  
1 5

<210> 40  
<211> 7  
<212> PRT  
<213> synthetic construct

<220>

<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (7)..(7)  
<223> AMIDATION

<400> 40

Tyr Xaa Phe Phe Tyr Pro Ser  
1 5

<210> 41  
<211> 7  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (7)..(7)  
<223> AMIDATION

<400> 41

Tyr Xaa Trp Phe Tyr Pro Ser  
1 5

<210> 42  
<211> 7  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (4)..(4)  
<223> Phe is Phe(pNO2), i.e. 4-nitrophenylalanine

<220>  
<221> MOD\_RES  
<222> (7)..(7)  
<223> AMIDATION

<400> 42

Tyr Xaa Trp Phe Tyr Pro Ser  
1 5

<210> 43  
<211> 7  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (6)..(6)  
<223> Nle

<220>  
<221> MOD\_RES  
<222> (7)..(7)



<223> AMIDATION

<400> 43

Tyr Xaa Phe Phe Leu Leu Asp  
1 5

<210> 44

<211> 3

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 44

Tyr Xaa Phe  
1

<210> 45

<211> 3

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (3)..(3)

<223> AMIDATION

<400> 45

Tyr Xaa Phe  
1

<210> 46  
<211> 3  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinoline  
n

<220>  
<221> MOD\_RES  
<222> (2)..(3)  
<223> nonpeptidyl bond

<400> 46

Tyr Xaa Phe  
1

<210> 47  
<211> 4  
<212> PRT  
<213> synthetic construct

<220>  
<221> MOD\_RES  
<222> (2)..(2)  
<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinoline  
n

<220>  
<221> MOD\_RES  
<222> (2)..(3)  
<223> nonpeptidyl bond

<400> 47

Tyr Xaa Phe Phe  
1

<210> 48

<211> 5

<212> PRT

<213> synthetic construct

<400> 48

Tyr Gly Gly Phe Met  
1 5

<210> 49

<211> 6

<212> PRT

<213> synthetic construct

<400> 49

Tyr Gly Gly Phe Met Lys  
1 5

<210> 50

<211> 6

<212> PRT

<213> synthetic construct

<400> 50

Tyr Gly Gly Phe Leu Lys  
1 5

<210> 51

<211> 6

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (1)..(1)

<223> NH2 of Tyr is blocked by butyloxycarbonyl group

<400> 51

Tyr Gly Gly Phe Leu Lys  
1 5

<210> 52

<211> 6

<212> PRT

<213> synthetic construct

<220>

<221> MOD\_RES

<222> (1)..(1)

*added* <223> NH2 of Tyr is blocked by butyloxycarbonyl group

<220>

<221> MOD\_RES

<222> (6)..(6)

<223> polymer connected to epsilon-amino group

<400> 52

Tyr Gly Gly Phe Leu Lys  
1 5